Digestive Diseases and Nutrition

The NIDDK supports a broad portfolio of basic, translational, and clinical research and training programs related to digestive diseases, which affect the gastrointestinal (GI) tract, pancreas, liver and biliary system, as well as nutritional disorders. They encompass some of the most common, severe, and disabling conditions afflicting Americans today. As illustrated in this chapter, past research supported by the NIDDK has enhanced our understanding of digestive system biology and function, and led to improvements in the health and well-being of people suffering from digestive and nutrition-related conditions. Given the impact on public health, the National Commission on Digestive Diseases recently assessed the state-of-the-science on digestive diseases and developed a long-range research plan, which was informed by a recent report on the current burden of digestive diseases in the U.S. The NIDDK will continue to foster new discoveries that advance the understanding, prevention, and treatment of digestive diseases and nutritional disorders.

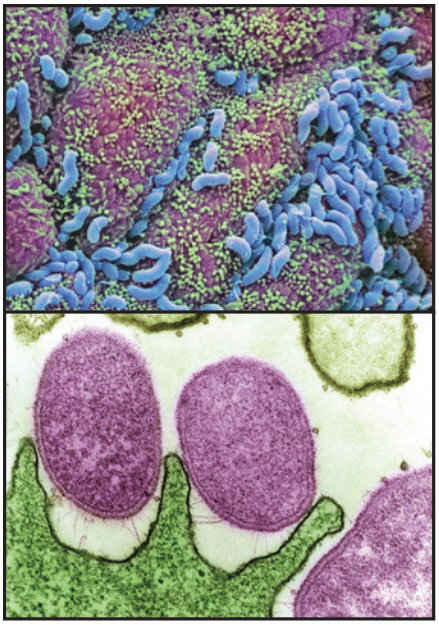
DISEASES OF THE GI TRACT

Targeting Acid Reflux and Related Diseases of the Esophagus: Gastroesophageal reflux disease (GERD), more commonly known as acid reflux or "heartburn," occurs when the stomach acid normally used to digest food flows backwards into the esophagus, resulting in inflammation, tissue damage, and associated conditions. The NIDDK has made significant investments over the years in research aimed at understanding the basic biology of acid production and secretion in the stomach. Nearly four decades ago, NIDDK-supported scientists discovered a "proton pump" on the surface of specialized cells responsible for the final step of acid secretion in the stomach. The methods developed to isolate the proton pump and study its biochemistry were critical for the design of new pharmacological agents that turn off the pump and block acid secretion. These so-called "proton pump inhibitors" are now the standard of care for the treatment of acid reflux and are amongst the most widely prescribed drugs on the market today.

GERD is associated with Barrett's Esophagus (BE), a condition in which cells lining the esophagus change in shape, organization, and function. BE puts patients at greater risk for developing esophageal adenocarcinoma, the predominant form of esophageal cancer in the U.S. The NIDDK supports research to identify risk factors and improve the treatment of BE. For example, in 2009, a landmark study conducted by a team of researchers throughout the country demonstrated the use of a new endoscopic procedure for the treatment of BE. In addition, NIDDK-supported studies identified behavioral risk factors associated with this condition. Researchers found that obesity, in particular an increased waist size, places individuals at greater risk of developing BE. However, a healthier diet that

includes more fruits and vegetables may help to reduce this risk. These studies and other continued efforts to identify genetic and epigenetic markers associated with BE will help to identify patients at risk, guide treatment protocols, and reduce the burden of diseases such as esophageal cancer.

Bacterial Contributions to Diseases of the Stomach: The discovery in the 1980s that the bacteria *Helicobacter pylori* resides in the human stomach and plays a role in the development of stomach inflammation, peptic ulcer disease, and gastric cancer revolutionized the understanding, management, and treatment of stomach diseases. In 1994, NIDDK convened an NIH Consensus Development Conference to assess the relationship between *H. pylori* and gastric malignancies. Following an evaluation of the state-of-the-science, the Consensus Development Panel made recommendations for the use of antimicrobial agents to target *H. pylori* infection, changing the standard of care for peptic ulcer disease. In response to this recommendation, novel antimicrobial treatment protocols have been developed to effectively eradicate the bacteria from the harsh environment of the stomach and virtually eliminate subsequent risk of developing peptic ulcers caused by this microbe.



Colorized electron micrographs of *Helicobacter pylori* bacteria (on top in blue; on bottom in purple) in the human stomach. *Image credits:* Top image: David McCarthy/ Photo Researchers, Inc; bottom image: SPL/ Photo Researchers, Inc.

Related to this seminal advance, researchers have been intensely interested in understanding the molecular basis for how *H. pylori* infection leads from stomach inflammation to the development of peptic ulcers and stomach cancer. NIDDK-supported scientists uncovered the key molecules that allow *H. pylori* to attach to the surface of stomach cells to mediate infection and determined how particular bacterial proteins, or virulence factors, disrupt the normal shape and structure of cells lining the stomach. In other breakthroughs, researchers studying the genetic diversity of *H. pylori* strains have identified different bacterial genes associated with the transition from simple inflammation to more serious pre-cancerous conditions and gastric cancer. Ongoing research will address how these genetic variations and virulence factors lead to the development of severe gastric disease and offer new avenues for the design of therapeutic interventions.

Intestinal Health and Disease: NIDDK research has illuminated the workings, in health and disease, of the body's "inner tube"—the intestines—where life-sustaining nutrients from foods are digested by enzymes secreted by the GI tract, pancreas, and beneficial resident bacteria into molecules that can be absorbed. Intestinal health problems, such as acute diarrhea, can be caused by "bad" bacteria or viruses that invade the intestines, and the NIDDK has supported research elucidating the mechanisms by which certain types of foodborne *Escherichia coli* cause severe diarrhea. Diarrhea can also be a symptom of intestinal diseases and functional bowel disorders.

Irritable bowel syndrome (IBS) causes severe, sometimes debilitating, intestinal pain, and occurs more often in women than in men. While diet and stress contribute to this disorder, the underlying causes are unknown. NIDDK-supported researchers are studying the interplay of gut and brain pathways in these disorders. For example, investigators found that women with IBS perceive visceral pain associated with this disorder differently than do healthy volunteers. They also found that a history of physical abuse heightens visceral pain responses in women with IBS. Additionally, researchers identified sex/gender-specific

differences in brain activity in female and male IBS patients. These findings may lead to the development of improved treatment strategies.

Celiac disease—an intolerance of the gluten proteins in many grains—causes intestinal damage and often goes undetected, which can result in malnutrition and impaired growth in children. Scientists have recently developed a test for proteins made by patients with celiac disease that permits earlier diagnosis.

In celiac disease, intestinal damage results from an intolerance to the gluten protein found in grains. *Image credit:* Illustration courtesy of the NIH Office of Medical Applications of Research.

Based on research findings, inflammatory bowel diseases (IBD) are thought to arise from genetic factors that cause inappropriate immune responses to otherwise harmless gut microbes. The two major types of IBD are Crohn's disease, which can occur in the small intestine and colon, and ulcerative colitis (discussed below), which occurs only in the colon. More than 30 IBD susceptibility genes have now been identified by research groups such as the NIDDK-supported IBD Genetics Consortium, a team of researchers from several sites in the U.S. and Canada. Many of the genes affect both forms of IBD, and their identification provides insights into disease processes and potential therapeutic targets. A timeline of NIDDK's major scientific advances in IBD research appears later in this chapter.

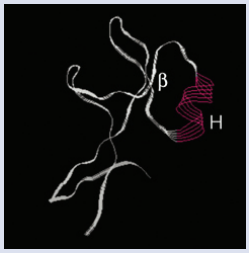
Diseases of the Colon: A common form of digestive disease in the U.S., colon cancer can be avoided if pre-cancerous polyps are identified during colorectal screening and removed. A 2008 NIDDK-supported study matching polyp size with pre-cancerous or cancerous states informed the development of updated guidelines for screening and management of colon cancer in the U.S. Another recent study focused on racial disparities in colon cancer and showed that African Americans had greater numbers of pre-cancerous polyps than Caucasians. Additionally, older adults were more likely to have polyps in the upper (proximal) colon, a region that can be evaluated by colonoscopy but not by sigmoidoscopy. These results may lead to further consideration of screening guidelines. In another area of research, a study of ulcerative colitis showed that the drug rosiglitazone reduced disease—first in mice, then in humans—and led to its being the first effective drug specifically indicated for this disease.

HIGHLIGHTS OF NIDDK-SUPPORTED IBD RESEARCH ADVANCES

1979: In the landmark National Cooperative Crohn's Disease Study conducted with principal support by the NIDDK, two pharmaceutical agents—prednisone and sulfasalazine—are each shown to be effective as treatments for Crohn's disease.

1994: Genetically engineered rats raised in a germ-free environment are found to be resistant to developing IBD in an NIDDK-supported study, suggesting that both microbes and genetic factors contribute to this disease.

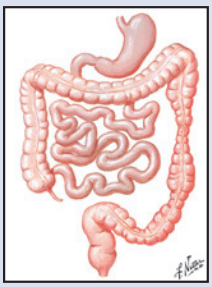
1994: In NIDDK-supported research, trefoil peptides are associated with wound healing in the intestine. More continues to be discovered about their key roles in mucosal tissue protection and repair, advancing understanding of IBD.



Trefoil factor 1 peptide
Image credit: Taupin D. and Podolsky D.K. Reprinted by permission from Macmillan Publishers Ltd: *Nat Rev Mol Cell Biol*, 4: 721-732, copyright 2003.

1999: TNF-alpha blocker infliximab approved for treating IBD. Research on using this new-generation drug to treat Crohn's disease was propelled by model mouse studies sponsored by the Institute.

2001: Discovery of first Crohn's disease susceptibility gene, *NOD2*. This landmark finding, by NIDDK-supported scientists, also identifies one of the first genes associated with a complex genetic disease and provides evidence linking IBD to an inflammatory response to bacteria.



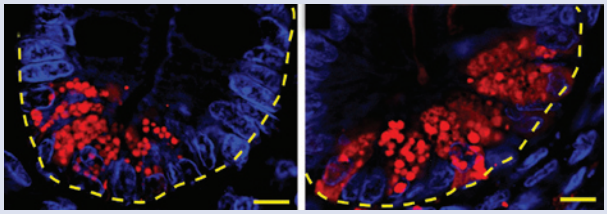
Artistic representation of the human digestive tract.
Image credit: Netter medical illustration used with permission of Elsevier. All rights reserved. http://www.netterimages.com.

2005: Two new mouse models developed with NIDDK support shed light on the protective role that the Crohn's disease susceptibility gene *NOD2* normally plays in fighting bacterial infection in the gut.

2006: NIDDK-funded researchers identify the *IL23 receptor* gene as a major Crohn's disease susceptibility gene.

2007: A subset of immune cells (T_H17 cells) is identified by NIDDK-supported researchers as inducing intestinal inflammation in Crohn's disease.

2007: In further NIDDK-supported genetic studies, the *ATG16L1* gene is associated with Crohn's disease, linking the cellular process of "autophagy" to IBD.



Autophagy gene *ATG16L1* expression in human intestinal cells
Image credit: Cadwell K et al. Reprinted by permission from Macmillan Publishers Ltd: *Nature*, 456: 259-263, copyright 2008.

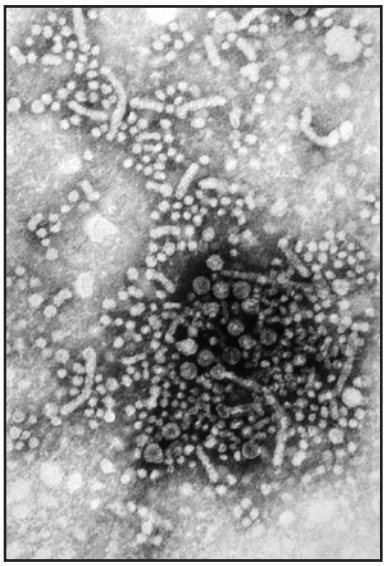
2008: NIDDK-funded trial of the diabetes drug rosiglitazone for ulcerative colitis demonstrates the short-term effectiveness of this treatment.

PRESENT: More than 30 IBD susceptibility genes have now been identified through collaborative studies conducted by international research groups, including the NIDDK-funded IBD Genetics Consortium.

Image credit: Image courtesy of Dr. Judy Cho, Yale School of Medicine, IBD Genetics Consortium.

HEPATOBILIARY DISEASES

Viral Hepatitis: Viral hepatitis is the most common cause of liver disease in the U.S. and worldwide. The NIDDK supports research to characterize and develop means of prevention, treatment, and control of the five major forms of viral hepatitis (hepatitis A, B, C, D, and E)—efforts which have led to direct health benefits for individuals affected by these diseases. Many past studies have focused on chronic hepatitis B and C, which are major causes of cirrhosis and liver cancer. Building on the Institute's basic research efforts to characterize the hepatitis B virus, including the Nobel-winning discovery of the virus by an NIDDK scientist in 1963, vaccination and blood screening programs have significantly reduced transmission of hepatitis B in the U.S. (See also the feature on Nobel laureates in this book.) The NIDDK has also sponsored long-term clinical trials to test the safety and compare the effectiveness of multiple drugs currently available to treat chronic hepatitis B. With centers throughout the country, the NIDDK-funded Hepatitis B Clinical Research Network will further advance understanding of disease processes and effective approaches to treating and controlling hepatitis B. Research on hepatitis C has also led to significant breakthroughs. Clinical studies by NIDDK intramural scientists in the 1980s tested the first effective treatment for chronic hepatitis C—long-term interferon therapy—which remains a standard treatment for the disease today. Additional clinical trials over the past decade have assessed the effectiveness of long-term hepatitis C treatment in preventing liver disease progression, tested therapies for chronic hepatitis C in children, and investigated different treatment responses in African Americans compared to Caucasians with chronic hepatitis C. NIDDK researchers also developed some of the first cell culture systems for studying the hepatitis C virus in the laboratory, enabling an expanded range of studies on viral life cycle and response to new antiviral agents.



Transmission electron micrograph showing particles of the virus that causes hepatitis B, a major form of liver disease. *Image credit:* CDC/ Betty Partin.

"God, I'm lucky," says **Howard Klein**, a musician who participated in several NIDDK clinical trials over the years to test various treatments against hepatitis B. A treatment stemming from these trials has allowed him to avoid serious disease and continue his music career.

Advances in Nonalcoholic Fatty Liver Disease (NAFLD) Research: NAFLD results from the inappropriate accumulation of fat in the liver, which can lead to more serious complications of liver injury, steatohepatitis (inflammation), and cirrhosis. NIDDK is pursuing research to understand basic mechanisms of fat metabolism in the liver and to develop ways to prevent and treat NAFLD. In recent years, NIDDK-supported scientists discovered how a cellular protein unexpectedly regulates production of fat in the liver and also uncovered a gene variant that may help to identify patients at risk for developing NAFLD. To combat the rise in NAFLD associated with increasing overweight and obesity in U.S. adults and children, NIDDK is conducting clinical trials of potential treatments for NAFLD within its multi-center Nonalcoholic Steatohepatitis Clinical Research Network. The

ongoing efforts of the Network's investigators are expected to uncover new information about disease development, broaden treatment options, and improve patient outcomes.

Gallstones: Gallstones are among the most common digestive disorders in the U.S., exacting high healthcare costs from their surgical treatment through gallbladder removal. From the 1960s to 1980s, NIDDK-supported investigators demonstrated how the normal physical and chemical properties of bile rely on maintaining cholesterol and calcium dissolved in the bile and described how alterations in this process led to gallstone formation. Animal models of cholesterol gallstones have been created, including strains of inbred mice that enabled the identification of several genetic factors that contribute to the disorder; some of these factors have been identified in humans as conferring increased susceptibility. Research also found that infection with several species of *Helicobacter* bacteria is associated with gallstone formation. Population studies showed that American Indian populations in several parts of the U.S. suffer from gallstones at a much higher rate than other racial or ethnic groups in this country.

Iron Metabolism and Hemochromatosis: Iron is essential for good health, but too much iron—a condition called iron overload—can threaten health by damaging organs, such as the liver and heart. Unfortunately, the human body does not have a natural way to rid itself of excess iron. Iron overload occurs in a disease called hemochromatosis, in which genetic mutations alter mechanisms that would otherwise precisely regulate iron absorption. NIDDK-sponsored research has advanced understanding of the causes of hemochromatosis and is contributing to improvements in its diagnosis and treatment. In the mid-1990s, scientists achieved a major advance in understanding hemochromatosis: they identified mutations in a gene called *HFE* that underlie the most common form of the disease in humans. Through further exploration, the scientists found that most of the people with mutant *HFE* genes do not develop clinical symptoms or signs of organ toxicity—indicating that additional mutations or environmental factors likely contribute to the development of hereditary hemochromatosis.

Joe Crossan has a disease called hemochromatosis, which causes a build-up of iron in his body. Fortunately, a treatment called phlebotomy helps people like Joe by removing excess iron from the circulation. Joe states "Thirty years ago, when my father died, very little was known about hemochromatosis. Thanks to research, a lot is known today about the disease."

Other insights into hemochromatosis emerged from studies showing the significance of the protein hepcidin in controlling iron balance in the body. The NIDDK continues to pursue these studies of iron metabolism, as well as to seek new diagnostic and therapeutic options for hemochromatosis, such as a non-invasive test to measure body iron and better iron chelators to remove excess iron from the blood.

Rare Genetic and Metabolic Liver Diseases: Alpha-1 antitrypsin deficiency is a rare genetic disease affecting children and adults. NIDDK-supported research has led to greater understanding of this disease, which is caused by mutations in the alpha-1 antitrypsin protein. These mutations cause the protein to be misshapen (or "misfolded") and to accumulate in the liver. Through experiments with mice and cells grown in the laboratory, researchers gained insights into which cellular processes are involved in the degradation and disposal of the mutant proteins, implicating pathways known as the "autophagy" pathway and the "ER overload response." By studying genes that were turned on or off to regulate disposal of mutant proteins, they also identified a gene activated in response to the aggregation of mutant alpha-1 antitrypsin proteins. This gene may be a new biomarker for research on disease development and progression and a potential target for new therapeutic strategies. Recently, researchers developed a new model for studying the

disease: a tiny transparent worm with mutant alpha-1 antitrypsin genes fused to a green fluorescent protein gene. The green proteins made from these genes can be observed aggregating within the liver or being secreted into the intestine. The scientists are currently adapting this little worm model for research to identify potential genetic modifiers of disease severity and for screening potential therapies for the disease.

Allen Russell's liver and lungs were being destroyed by alpha-1 antitrypsin deficiency when a liver transplant saved his life. Allen says, "I remain extremely grateful to my donor for my second chance in life." NIDDK is dedicated to improving the care of people with this disease by supporting research to advance liver transplantation and develop new treatments.

Liver Transplantation-related Topics: Since the first human liver transplantation was performed in 1967 by an NIDDK grantee, the Institute has supported research to improve outcomes of this potentially life-saving procedure for those with severe liver disease and/or acute liver failure. For example, NIDDK research contributed to surgical and organ preservation techniques that reduce patient blood loss, preserve the donor organ, and lengthen the time available for organ transportation and surgery. Research has also provided evidence for development of effective post-operative immunosuppressive therapy to prevent liver transplant rejection. The NIDDK played a key role in organizing an NIH Consensus Development Conference on liver transplantation held in 1983 that supported the use of this procedure for end-stage liver disease, prompting a dramatic increase in the number of liver transplants performed in the U.S. The Institute continues to support research efforts to enhance liver transplantation through such programs as the Adult-to-Adult Living Donor Liver Transplantation Cohort Study (A2ALL), conducted by a group of researchers throughout the country. In the last few years, A2ALL has characterized the benefits and risks of the living donor liver transplantation procedure for donors and for recipients, including specific patient populations such as those with hepatitis C. Another NIDDK-supported program called Studies of Pediatric Liver Transplantation conducts research to improve the success of liver transplants in children.

The NIDDK also supports research on some of the conditions that commonly lead to liver transplantation, such as drug-induced liver injury and resulting acute liver failure, through programs such as the Drug-Induced Liver Injury Network and both the adult and pediatric Acute Liver Failure Study Groups, all conducted at multiple sites across the country. These programs are assessing ways to better detect, treat, and prevent severe liver injury due to drugs (prescription and over-the-counter) or complementary and alternative medicines, so that individuals do not reach the point of requiring a liver transplantation.

HIGHLIGHTS OF NIDDK-SUPPORTED LIVER RESEARCH ADVANCES

1963: An NIDDK intramural scientist discovers hepatitis B virus or "Australia antigen" while conducting research at the Institute, for which he is subsequently awarded the Nobel Prize in Physiology or Medicine. This finding represents a scientific and clinical breakthrough in detection and control of viral hepatitis and leads to the development of measures to prevent viral hepatitis and liver cancer.

1967: The first human liver transplantation is performed by an NIDDK grantee. This surgical breakthrough opens the door for use of this life-saving procedure in cases of severe liver disease and acute liver failure.

1983: NIH Consensus Development Conference on liver transplantation, sponsored by the NIDDK and NIH Office of Medical Applications of Research, supports use of this procedure for end-stage liver disease, prompting a dramatic increase in the number of liver transplants performed in the U.S.

1986: Clinical research conducted by intramural scientists in the NIDDK Liver Diseases Section provides evidence for the first effective treatment for chronic hepatitis C in the form of long-term interferon therapy.

1998: NIDDK-supported researchers develop a mouse model of hereditary hemochromatosis by knocking out the *HFE* gene. This animal model also confirms the importance of *HFE* to the development of hepatic iron overload in this disease.

2002: The NIDDK-supported Adult Acute Liver Failure Study Group reports that liver injury is increasing in the U.S. due to overdose of the painkiller acetaminophen, which is now the leading cause of acute liver failure.

2005: NIDDK intramural researchers develop some of the first cell culture systems to study hepatitis C virus *in vitro*, enabling direct laboratory investigation of viral life cycle and response to antiviral agents.

2007: A mouse model is developed with a "humanized" liver by replacing the livers of immunodeficient mice with human liver cells. This animal model can be used in the future to facilitate new drug development and research in such areas as drug-induced liver disease, viral hepatitis, and liver regeneration.

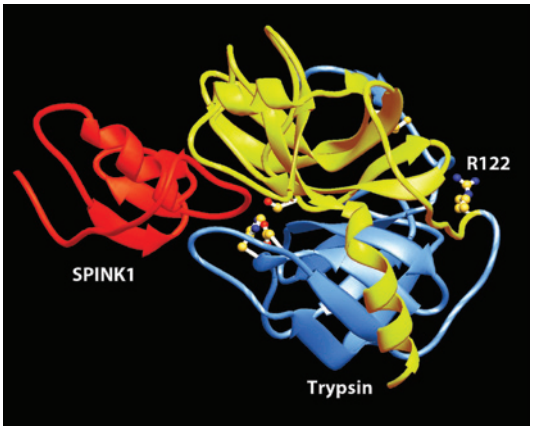
2007-2008: The NIDDK-supported Adult-to-Adult Living Donor Liver Transplantation Cohort Study (A2ALL) characterizes the benefits and risks of the living donor liver transplantation procedure for both recipients and donors.

2008: Results of the NIDDK-funded clinical trial called Hepatitis C Antiviral Long-term Treatment against Cirrhosis (HALT-C) demonstrate that, in people who do not respond to initial therapy, longer-term interferon treatment is ineffective in preventing chronic hepatitis C progression to conditions such as cirrhosis and liver cancer, emphasizing the importance of developing other long-term therapeutic approaches.

2008: NIDDK provides leadership for the NIH Consensus Development Conference on Management of Hepatitis B and launches the Hepatitis B Clinical Research Network.

DISEASES OF THE PANCREAS

Genetic Insights into Pancreatitis: Pancreatitis, or inflammation of the pancreas, is believed to result from destruction of the pancreas from the inside, by the digestive enzymes that it produces. In 1996, NIDDK-supported scientists reported the discovery of a genetic variant in patients suffering from hereditary pancreatitis. The mutation is in the gene encoding a form of trypsin, a digestive enzyme which is normally inactive in the pancreas, and which self-destructs if prematurely activated to avoid pancreatic damage. The mutation disables this defense mechanism. Subsequent studies identified other genetic variants associated with pancreatitis, including mutations in a gene that helps protect the pancreas from trypsin activity, and in the *CFTR* gene, originally identified in association with cystic fibrosis. In an ongoing study with participants from the North American Pancreatic Study Group, researchers are scanning entire genomes to uncover other genetic markers that may help to identify susceptible individuals and prevent pancreatitis.



Ribbon diagram of the trypsinogen-trypsinogen inhibitor complex; a mutation in the trypsinogen gene is associated with hereditary pancreatitis.
Image credit: Image courtesy of Dr. David Whitcomb.

Uncovering a Genetic Cause of Zollinger-Ellison Syndrome (ZES): Patients with ZES have tumors in the pancreas and small intestine, which release hormones that trigger overproduction of stomach acid and formation of peptic ulcers. Some of these tumors are caused by an inherited genetic disorder called multiple endocrine neoplasia type 1 (MEN1). Scientists at the NIDDK, including former NIDDK Director Dr. Allen Spiegel, in collaboration with a team of scientists at the National Human Genome Research Institute led by Dr. Francis Collins, now the NIH Director, were the first to clone the *MEN1* gene and identify several mutations associated with this inherited disorder (see also Intramural chapter). Subsequently, researchers discovered that *MEN1* produces a protein that acts as a "tumor suppressor" to suppress cell growth. As these landmark studies uncovered the molecular basis of ZES caused by MEN1, the NIDDK continues to lead innovative studies aimed at improving approaches to the diagnosis and management of ZES.

NUTRITION AND METABOLISM

Many health conditions are affected by nutrients in the foods we consume, and how well our bodies metabolize these nutrients. In addition to research on diabetes, metabolic disorders, and obesity, which are described in greater detail in other chapters of this book, the NIDDK supports studies related to other specific nutritional and metabolic alterations. For example, researchers investigating metabolism of the nutrient copper, which plays an essential role in many biological processes as an enzyme component, uncovered some of the mechanisms and potential therapeutic targets associated with an inherited form of copper deficiency called Menkes disease. Children with this disease suffer from seizures, poor muscle tone, neurodegeneration, and failure-to-thrive starting a few weeks after birth. NIDDK-supported research using a zebrafish model has enhanced knowledge of how Menkes disease develops and can best be treated.

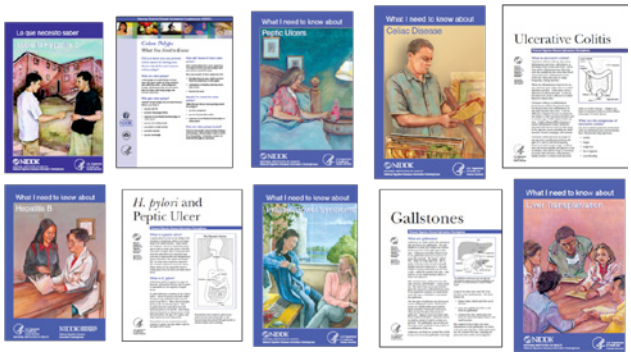
CROSS-CUTTING DIGESTIVE DISEASES AND NUTRITION-RELATED RESEARCH

Many areas of NIDDK-supported research cut across multiple digestive diseases and nutritional disorders. For example, through genomic studies, researchers have uncovered genetic variants associated with several digestive diseases, such as hereditary pancreatitis, celiac disease, Crohn's disease, and nonalcoholic fatty liver disease. Scientists are also studying, through programs

such as the NIH Human Microbiome Project, how the composition of bacteria that reside in the gut influences digestive health. NIDDK-supported studies have led to important discoveries of how the gut microbial community contributes to conditions such as IBD and potentially to obesity. NIDDK-funded researchers are also investigating other factors in the gut that contribute to obesity, and uncovering, for example, how a hormone released in the gut increases the feeling of hunger in the brain. Investigators in the multi-center Longitudinal Assessment of Bariatric Surgery (LABS) and related Teen-LABS studies are assessing long-term risks and benefits of bariatric surgery in adults and adolescents. Many other avenues of obesity research are described in the Obesity chapter.

Mariah Watts suffered from sleep apnea, a dangerous condition associated with obesity, had pre-diabetes, and tried many weight loss approaches that didn't work. As a last resort, she underwent bariatric surgery, after assessment by a multidisciplinary pediatric clinical team to determine her eligibility, and her health has improved. Having researched the procedure on her own on the internet, she suggests that others "do their homework first" too, before deciding on surgery. Mariah is participating in Teen-LABS, an observational study collecting data from just before surgery to two years after, to evaluate the surgery's risks and benefits — information that will help others. Her mother says, "We thought it was important for us to get involved so that other parents and their teenage children could make more informed decisions." Mariah agrees.

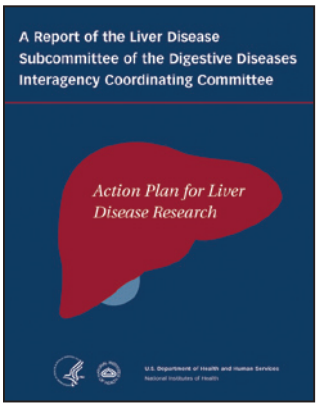
EDUCATION PROGRAMS



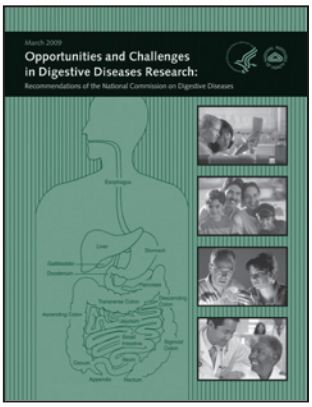
Information from the National Digestive Diseases Information Clearinghouse.

The NIDDK supports education programs for patients, their families, healthcare providers, and the public to enhance knowledge of digestive and nutrition-related conditions and prevention and treatment approaches. For example, many people are unaware they have celiac disease, an intolerance to the protein gluten found in some grains, which can result in intestinal injury and reduced nutrient absorption. Although an effective treatment exists in the form of a gluten-free diet, celiac disease often goes undiagnosed and thus untreated. The Celiac Disease Awareness Campaign was launched by the NIDDK in 2006 in response to recommendations from a 2004 NIH Consensus Development Conference to provide a variety of informational materials. Another educational campaign is being developed to address the rising rate of fecal incontinence in the aging U.S. population. This campaign to educate professionals and the public stems from recommendations of a 2007 NIH State-of-the-Science Conference. The National Digestive Diseases Information Clearinghouse, established in 1980, provides a variety of user-friendly educational materials about digestive diseases to patients, their families, health professionals, and the public, including clinical trial information, print and web-based publications, listings of patient organizations, and interactive health features and tools. Clearinghouse materials, in English and Spanish, can be accessed electronically or ordered in hard copy at http://digestive.niddk.nih.gov/.

LOOKING TO THE FUTURE



Trans-NIH *Action Plan for Liver Disease Research*
U.S. Department of Health and Human Services, National Institutes of Health, December 2004, NIH Publication No. 04-5491.



Opportunities and Challenges in Digestive Diseases Research: Recommendations of the National Commission on Digestive Diseases
U.S. Department of Health and Human Services, National Institutes of Health, March 2009, NIH Publication No. 08-6514.

Tomorrow's research directions for digestive and nutrition-related diseases are informed by a combination of ongoing efforts, including strategic plans, workshops, broad external input from stakeholders—along with the fruits of current research—with the ultimate aim of improving the lives of patients and their families. The NIDDK has provided substantial leadership and support for important trans-NIH research planning efforts related to digestive diseases. The trans-NIH *Action Plan for Liver Disease Research*, released in 2004, identifies areas of scientific opportunity leading to research goals in the prevention and control of liver and biliary diseases. Another research plan, entitled *Opportunities and Challenges in Digestive Diseases Research: Recommendations of the National Commission on Digestive Diseases*, released in 2009, is the culmination of a rigorous 4-year planning process to identify research challenges and opportunities spanning the wide range of digestive conditions. Within the Commission's research plan, a chapter on liver and biliary diseases references and updates research goals from the *Action Plan*. Both the liver disease-focused and the broader digestive diseases research plans feature a 10-year time horizon and represent the broad external input of individuals committed to advancing digestive diseases research, including those from the NIH and other Federal agencies, intramural and extramural researchers, physicians, and representatives of professional and patient advocacy groups. These research plans can be accessed in electronic form or ordered in hard copy through the following web sites: http://liverplan.niddk.nih.gov and http://NCDD.niddk.nih.gov.

Photo credit: Richard Nowitz, for NIDDK.